thyroxine receptor.

128. (New) The method of claim 124 or 125, wherein the detectable thyroxine is labeled with a detectable marker.

129. (New) The method of claim 123, wherein a concentration lower than 0.3 ng/ml or a concentration higher than 1.5 ng/ml indicates that the subject is not receiving the proper dosage of thyroxine.

**REMARKS**

Claims 1, 2, 9-11, 17-19, 25-27, 33-35, 41, 42, 47, 48, 54, 55, 60, 61, 67, 68, 74-76, 81-83 and 88 are pending in the subject application. By this Amendment, applicants have cancelled claims 1, 2, 25-27, 54, 55, 60, 61 and 81-83 without prejudice or disclaimer and added new claims 94-129. New claims 94-129 correspond to canceled claims 1-8, 25-32, 54-66 and 81-87, respectively. Applicants maintain that the addition of new claims 94-129 raises no issue of new matter and is fully supported by the specification as filed. Applicants respectfully request that this Amendment be entered.

Upon entry of this Amendment, claims 9-11, 17-19, 33-35, 41, 42, 47, 48, 67, 68, 74-76, 88 and 94-129 will be pending, and claims 33-35 and 94-129 will be under examination.

Applicants note that claims 33-35, though not restricted into any group by the Examiner in the November 5, 2002 Office Action, are still pending, and presumed to be under examination.

**Restriction Requirement**

In the Office Action, the Examiner restricted the pending claims to one of the following allegedly distinct inventions under 35 U.S.C. §121:

I. Claims 1-2, 25-27, 54-61 and 81-83, drawn to a method of diagnosing a thyroid condition, determining a concentration of TSH and thyroxine;

II. Claims 9-11, 41-48 and 74-76, drawn to a method of diagnosing a thyroid condition and whether a person treated with thyroxine is receiving proper dosage, determining a concentration of triiodothyronine and TSH;

III. Claims 67-68 and 88, drawn to a method of determining whether a subject being treated with thyroxine is receiving a proper dosage and a method of monitoring the subject, determining TSH; and

IV. Claims 17-19, drawn to a method of diagnosing a thyroid condition, determining a concentration of triiodothyronine-sulfate.

In response, applicants hereby elect, with traverse, Group I, claims 1-2, 25-27, 54-61 and 81-83. As applicants have herein cancelled claims 1-2, 25-27, 54-61 and 81-83 and added claims 94-129 corresponding to these claims as well as previously canceled claims depending therefrom, applicants understand that claims 94-129 will be under examination upon entry of this Amendment.

Applicants respectfully request that the Examiner reconsider and withdraw the restriction requirement. Under 35 U.S.C. §121,

restriction may be required if two or more independent and distinct inventions are claimed in one application. Under M.P.E.P. §803, the Examiner must examine the application on the merits, even though it includes claims to distinct inventions, if the search and examination can be made without serious burden.

The inventions of Groups I-IV are not independent. Under M.P.E.P. §802.01, ''independent'' means there is no disclosed relationship between the subject matter claimed. The inventions of Groups I-IV all relate to methods of diagnosing a thyroid condition and methods of determining whether subjects treated with thyroxine are receiving a proper dosage of thyroxine. Applicants maintain their position is underscored by the fact that Groups I and II belong to the same class and subclass. Applicants therefore maintain that groups I-IV are not independent and restriction is not proper.

Furthermore, under M.P.E.P. §803, the Examiner must examine the application on the merits if examination can be made without serious burden, even if the application would include claims to distinct or independent inventions. That is, there are two criteria for a proper requirement for restriction: (1) the invention must be independent and distinct, and (2) there must be a serious burden on the Examiner if restriction is not required.

Applicants respectfully submit that there would not be a serious burden on the Examiner if restriction were not required, because a search of the prior art relevant to the claims of Groups II-IV would not require a serious burden once the prior art relevant to Group I has been identified. Therefore, there would be no serious burden on the Examiner to examine Groups I-IV together in the subject application. Hence, the Examiner must examine these Groups on the merits.

In view of the foregoing, applicants maintain that restriction is

not proper under 35 U.S.C. §121 and respectfully request that the Examiner reconsider and withdraw the requirement for restriction.

**Supplemental Information Disclosure Statement**

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (**Exhibit A**). Copies of the disclosures listed below as items 1-29 are attached hereto as **Exhibits 1-29**, respectively.

1. Burke, C.W, et al. (1972) "Measurement of Thyroxine and Triiodothyronine in Human Urine," The Lancet, 1177-1179 (**Exhibit 1**);

2. Chan, V., et al. (1972) "Urinary Tri-Iodothyronine Excretion as Index of Thyroid Function," The Lancet, 253-256 **(Exhibit 2)**;

3. Chandler, J., et al. (2000) "The Place of Gold in Rapid Tests," IVD Technology, 37-49 **(Exhibit 3 )**;

4. Danese, M.D., et al. (1996) "Screening for Mild Thyroid Failure at the Periodic Health Examination," JAMA 276 (4): 285-292 **(Exhibit 4)**;

5. Faber, J., et al. (1981) "Urinary Excretion of Free and Conjugated 3', 5'-Diiodothyronine and 3', 3'-Diiodothyronine," Journal of Clinical Endocrinology and Metabolism 53 (3): 587-593 **(Exhibit 5)**;

6. Gaitan, J.E., et al. (1975) "Measurement of

Triiodothyronine in Unextracted Urine," J. Lab. Clin. Med. 86: 538-546 **(Exhibit 6)**;

7. Hertz, S., et al. (1936) "Assay of Blood and Urine for Thyreotropic Hormone in Thyrotoxicosis and Myxdema," Endocrinology 20 (4): 520-525 **(Exhibit 7)**;

8. Hufner, M., et al. (1973) "Tri-Iodothyronine Determinations in Urine," The Lancet 101-102 **(Exhibit 8)**;

9. Kuku, S.F., et al. (1971) "Concentrations of Immunoreactive Thyrotropic Hormone in Urine of Normal Subjects, Patients with Thyroid Disorders and Hypopituitarism and After Infusion of Human Thyrotropic Hormone," J. Endocr. 62: 645-655 **(Exhibit 9)**;

10. Nelson, J.C., et al. (1996) "Analytical Performance of Free and Total Thyroxine Assays," Clinical Chemistry 42 (1): 146-154 **(Exhibit 10)**;

11. Nelson, J.C., et al. (1994) "Variable Underestimates by Serum Free Thyroxine ($T_4$) Concentrations in Simple Solutions," Journal of Clinical Endocrinology and Metabolism 79 (5): 1373-1375 **(Exhibit 11)**;

12. Orden, I., et al. (1987) "Thyroxine in unextracted Urine," Acta Endocrinologica 114: 503-508 **(Exhibit 12)**;

13. Singer, P.A., et al. (1995) "Treatment Guidelines for Patients with Hyperthyroidism and Hypothyroidism," JAMA 273 (10): 808-812 **(Exhibit 13)**;

14. Stockigt, J.R. (2000) "Serum Thyrotropin and Thyroid Hormone Measurements and Assessment of Thyroid Hormone Transport," The Thyroid: A Fundamental and Clinical Text 376-392 **(Exhibit 14)**;

15. Surks, M.I., et al. (1972) "A New Radioimmunoassay for Plasma L-Triiodothyronine: Measurements in Thyroid Disease and in Patients Maintained on Hormonal Replacement," The Journal of Clinical Investigation 51: 3104-3113 **(Exhibit 15)**;

16. Tunbridge, W.M., et al. (1977) "The Spectrum for Thyroid Disease in a Community: The Whickham Survey," Clinical Endocrinology 7: 481-493 **(Exhibit 16)**;

17. Van Herle, A.J., et al. (1978) "Immunoreactive 'TSH' in Urinary Concentrates of Graves' Disease Patients: a Radioimmunoassay Artefact," Eur. J. Clin. Invest. 8: 295-301 **(Exhibit 17)**;

18. Vanderpump, M.P.J., et al. (1995) "The Incidence of Thyroid Disorders in the Community: A Twenty-Year Follow-Up of the Whickham Survey," Clinical Endocrinology 43: 55-68 **(Exhibit 18)**;

19. Wiczyk, H.P., et al. (1998) "Recognizing Thyroid Disease," The Female Patient 23: 67-80 **(Exhibit 19)**;

20. Yoshida, K., et al. (1988) "Measurement of Thyroid Stimulating Hormone (TSH) in Human Urine," Endocrinol. Japon. 35 (5): 733-739 **(Exhibit 20)**;

21. Yoshida, K., et al. (1980) "Measurement of Triiodothyronine in Urine," Tohoku J. Exp. Med. 132: 389-395 **(Exhibit 21)**;

22. European Patent Application No. EP 0 653 639 A1, filed November 12, 1993 **(Exhibit 22)**;

23. European Patent Application No. EP 0 653 625 A1, filed November 7, 1994 **(Exhibit 23)**;

24. International Patent Application No. WO 95/13542, filed May 18, 1995 **(Exhibit 24)**;

25. International Patent Application No. WO 96/24060, filed August 6, 1995 **(Exhibit 25)**;

26. British Patent Application No. 9502112.7, filed February 3, 1995 **(Exhibit 26)**;

27. U.S. Patent No. 4,312,854, issued January 26, 1982 **(Exhibit 27)**;

28. U.S. Patent No. 4,410,633, issued October 18, 1983 **(Exhibit 28)**; and

29. The Colorado Thyroid Disease Prevalence Study, Archives of Internal Medicine 160.(4): 526-534 **(Exhibit 29)**.

Each of the above-listed publications is listed again on the accompanying PTO Form 1449 (**Exhibit A**).

Applicants request that the Examiner review the publications and make them of record in the subject application.

**Summary**

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed check for $510.00, including a $465.00 extension fee and a $45.00 additional claim fee, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

3/5/03
Alan J. Morrison Date
Reg. No. 37,399